EXHIBIT D

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION **THIS DOCUMENT RELATES TO WAVE 1 / TVT-R CASES**	**Master File No. 2:12-MD-02327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

RULE 26 EXPERT REPORT OF JERRY G. BLAIVAS, M.D.

The following report is provided pursuant to Rule 26 of the Federal Rules of Civil Procedure. My opinions are as follows:

I. QUALIFICATIONS

Dr. Blaivas is a board certified urologist in the state of New York. He attended Tufts College for his bachelor's degree in 1964 and Tufts University School of Medicine for his medical doctorate in 1968. He completed a urology residency in 1976 after completing a general surgery internship followed by a two year general surgery residency. He has been teaching medicine since 1976 at Tufts University School of Medicine, Columbia University, Cornell University and most recently, SUNY Downstate Medical School. Throughout his academic career, Dr. Blaivas remained a practicing surgeon in a number of hospitals in Massachusetts and New York, and is currently an attending surgeon at The New York Presbyterian Hospital and Lenox Hill Hospital.

Dr. Blaivas is one of the pioneers of sling surgery for women with sphincteric incontinence. He performed his first autologous rectus fascial sling operation in 1981 and shortly thereafter modified the technique by creating a fascial graft instead of a fascial flap which was the prevailing method at the time. The reason for this change is that the flap was tethered by its abdominal attachments such that it was very difficult to place the sling loosely enough to avoid causing urethral obstruction. Once that modification was adapted, it was much easier to place the sling without any tension at all and that principle became the guiding principle for the subsequent development of synthetic mesh slings. In 1998, Dr. Blaivas, in a peer review journal, proposed that rectus fascial sling be considered a suitable operation for all women with sphincteric incontinence. Prior to that time, it was considered to be indicated only in women with complicated problems who had failed prior incontinence operations.

In the 1980's, Dr. Blaivas became acquainted with severe complications that resulted from synthetic mesh slings composed of Marlex and Mersilene. He performed a number of surgeries to remove these slings because of severe, refractory complications including pain, infection, erosion and urinary fistula. So difficult and problematic were these complications that Dr. Blaivas traveled to Toronto and spent some time with Ted Morgan, MD – a gynecologist who performed the largest number of these operations in the peer review literature. Dr. Morgan was considered to be a highly qualified surgeon, but even in his hands devastating complications occurred and they often occurred years after the original surgery. In the hands of less skilled surgeons, the complication rate was much higher. Dr. Blaivas discussed the surgical technique of sling surgery and methods of treating complications in great detail with Dr. Morgan. He concluded that: 1) even in the hands of a master surgeon, devastating complications could occur with synthetic slings, but rarely if ever occurred with autologous fascial (graft) slings; 2) in the hands of inexperienced surgeons, the complication rate could be unacceptably high; 3) removal of the mesh was exceedingly difficult and fraught with its own complications; 4) once a complication occurred, the chances of a successful outcome are low; and 5) the mesh itself, because it is a foreign body, contributes significantly to the complication rate. Because of these known complications and the technical difficulties performing mesh surgery, the operation fell out of favor until synthetic slings were revived, reinvented and promoted by industry through pervasive advertising and inducements to physicians to perform such surgeries.

Dr. Blaivas himself was heavily "recruited" by manufacturers of synthetic slings to become a "key opinion leader" and promote sling surgery. He was thoroughly vetted by industry representatives and Peter Petros, MD, one of the pioneers of synthetic sling surgery, spent a week with him in New York at his office and in the operating room discussing and demonstrating the theory and surgical technique of synthetic sling surgery. It was during this period of time that Dr. Blaivas decided to perform some synthetic slings in highly selected patients because the procedure could be performed so quickly and with so small an incision. Once he became adept at the technique through simulated training, he realized that there really wasn't any need for the "sling kit" that was supplied by the manufacturer. Further, he thought that the technique of passing the trocars from the vagina upwards to the abdomen was a much more dangerous technique that could lead to adjacent organ injury. So, instead, he fashioned a strip of "Gynemesh" and used a Stamey needle to pass the trocars from the abdomen to the vagina. He further modified the technique to include dissection alongside the urethra into the retropubic space, nearly eliminating the possibility of injuring the bladder or urethra or adjacent organs with the trocars.

In essence, Dr. Blaivas was using exactly the same technique he used for rectus fascial slings (which was considered the gold standard for incontinence surgery) and simply replaced the rectus fascial graft with a synthetic graft. Dr. Blaivas considered that synthetic slings, using the technique described here, could actually improve sling surgery provided that the new meshes were improved to the point that they had an acceptable safety profile and, in fact, he opined that synthetic slings will become the standard once the bugs were worked out. But to date, that has not happened. Throughout this time (the last decade of the 20th and first decade of the 21st century), Dr. Blaivas became increasingly aware of devastating, life threatening, and life style altering complications of synthetic sling surgery and became a world renowned expert at treating those complications. He has personally operated on about 75 – 100 patients with severe synthetic mesh

complications, and taken care of hundreds more who either did not elect further surgery or who simply gave up and were seeking relief from pain management experts. He has also discussed these issues with his peers. It is that experience, supported by peer-reviewed scientific literature, which forms the basis of the following opinions.

In August, 2015, Dr. Blaivas published the review article, "Safety considerations for synthetic sling surgery" in Nature Reviews Urology. The Nature family of journals is regarded as one, if not *the* premier resource for scientific research in the world.[1] Publication in Nature Reviews Urology, requires that the article meet strict criteria.[2] In its final version, the article was a herculean project - naming nine authors, spanning 29 pages, and containing 397 references. The exhaustive research presented in this paper further supports the opinions.

All of these opinions are to a reasonable degree of medical certainty. He applied the same scientific rigor that he use in all aspects of his professional activities, including caring for patients, publishing, lecturing, consulting with other health care professionals, and serving as a litigation expert. The methodology he used in rendering my opinions is the same that he uses in his professional activities. His opinions have been consistent over time and do not differ just because they are provided for various purposes or audiences.

Dr. Blaivas' Curriculum Vitae is attached hereto and by reference made a part hereof. Please see Exhibit "A" attached.

II. DISCUSSION OF OPINIONS

1. The Gynecare TVT-R is a polypropylene mesh product made and marketed by Ethicon to allegedly treat stress urinary incontinence ("SUI"). The TVT-R was the first polypropylene midurethral sling made and marketed for treatment of SUI. It product consists of:

- PROLENE® polypropylene mesh (either Mechanically Cut Mesh ("MCM") or Laser Cut Mesh ("LCM")) with a polyethylene sheath or covering and attached trocars / surgical devices
- A TVT introducer
- A TVT Rigid Catheter Guide
- Instructions for use (IFU)

2. From the time it was introduced to the market through January 2015, the IFU for the TVT-R did not change. In January 2015, Ethicon introduced a new IFU with some modifications, as discussed below.

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[1] "The Nature Reviews clinical journals commission leaders in the field to write clinical content of the highest quality, authority and accessibility. Content is subject to rigorous review by our in-house editors and/or peer-review, and counsel is provided by the Editors-in-Chief and an international Advisory Boards to ensure comprehensive coverage of topical issues." Nature.com accessed 12/18/2015.

[2] The criteria for publication include: Timely, accurate and balanced; Important for practicing doctors, researchers and academics in the subspecialty; Interesting and accessible to practicing doctors, researchers and academics in wider specialties. Nature.com accessed 12/18/2015.

3. The Gynecare TVT should not have been designed for placement in a surgically contaminated field[3] without proper animal and clinical studies to document safety and without a clear warning about the possibility of short and long term complications.[4] Bacteria attaches to mesh during the insertion process and can cause both acute and chronic infections in women.[5] Infection, even subclinical, can result in chronic inflammation, scarring, pain, abscess, vaginal, bladder and urethral erosion and other complications.

4. The Gynecare TVT causes serious and life-style altering complications including but not limited to chronic pelvic pain syndromes, chronic dyspareunia and sexual impairment, nerve injuries, de novo urinary symptoms, infections, fistulas, urethral obstruction, urethral strictures, bladder stones, death, vaginal, urethral, and bladder erosions, pelvic organ dysfunction, pelvic anatomy distortion, and other complications. These complications often require reoperation and are sometimes permanent. Because of these complications, the risks of these devices outweigh the benefits. I also am aware of many complications including deaths, injury to the iliac artery and vein, bowel injury and ureteral injuries despite the fact that virtually none of these complications were reported in the peer review literature.[6] Many of these complications can occur many years or even decades after the original surgery.[7]

5. The management of many sling complications is fraught with complexity and results in a high rate of persistent symptoms.[8] This has been evident since the complications from the Mersilene, Marlex, Gore-Tex, and Protogen slings that were performed during the last three decades of the 20th century and more recently the Protegen and Mentor ObTape slings. Further Ethicon knew or should have known about the contemporaneous complications that were occurring with their devices and with the devices of their competitors. From a scientific and ethical perspective, Ethicon should have had a high index of suspicion relating to the product defects based on the previous experiences with other synthetic products. For retropubic synthetic slings,

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[3] E.g., Culligan P, Heit, M., Blackwell, L., Murphy, M., Graham, C. A., & Snyder, J. Bacterial colony counts during vaginal surgery. Infectious Dieseases in Obstetrics and Gynecology. 2003;11(3):161-5.

[4] E.g., Vollebregt A, Troelstra, A., & van der Vaart, C. H. . Bacterial colonisation of collagen-coated polypropylene vaginal mesh: are additional intraoperative sterility procedures useful? International Urogynecology Journal and Pelvic Floor Dysfunction.2009: 20(11):1345-51; Choi JJ, Palaniappa, N. C., Dallas, K. B., Rudich, T. B., Colon, M. J., & Divino, C. M. Use of Mesh During Ventral Hernia Repair in Clean-Contaminated and Contaminated Cases. Annals of Surgery. 2012;255(1):176-80.

[5] E.g., Vollebregt, 2009; Choi, 2012; Klinge U, Klosterhalfen, B., Muller, M., Ottinger, A. P., & Schumpelick, V. Shrinking of polypropylene mesh in vivo: an experimental study in dogs. The European Journal of Surgery. 1998;164(12):965-9.

[6] E.g.,Petri, 2012; Rogo-Gupta, 2013; Ross S, Robert M, Swaby C, Dederer L, Lier D, Tang S, et al. Transobturator tape compared with tension-free vaginal tape for stress incontinence: a randomized controlled trial. Obstetrics and gynecology. 2009;114(6):1287-94; Cholhan HJ, Hutchings TB, Rooney KE. Dyspareunia associated with paraurethral banding in the transobturator sling. American journal of obstetrics and gynecology.

[7] Boyles SH, Edwards R, Gregory W, Clark A. Complications associated with transobturator sling procedures. Int Urogynecol J Pelvic Floor Dysfunct. 2007;18(1):19-22; Parnell BA, Johnson EA, Zolnoun DA. Genitofemoral and perineal neuralgia after transobturator midurethral sling. Obstetrics and gynecology. 2012;119(2 Pt 2):428-31.

[8] E.g., Deng DY, Rutman, M., Raz, S., & Rodriguez, L.V. Presentation and management of major complications of midurethral slings: Are complications underreported? Neurourology and Urodynamics. 2007;26(1):46-52.

the most devastating complications are those that are due to vascular and bowel injuries and a number of deaths have been reported from these.[9]

6. The two most debilitating and challenging complication to treat are chronic pain and urinary fistulas. This pain can be located in the abdomen, pelvis, vagina, buttocks, perineum, groin, thigh, or leg. It can be acute (occurring immediately after surgery) or chronic with an insidious onset. It is often refractory to traditional treatments. It can be related to erosion; scarring; mesh deformation; entrapment or compression of large nerves with classic or atypical nerve distribution; entrapment of smaller nerve branches with diffuse distribution; muscular inflammation, scarring, trauma, and hypertonicity; visceral pain syndromes; and other complications. It can be associated with other sensory changes such as numbness and tingling.

7. Chronic Mesh Pain Syndrome (CMPS) has been described in the medical literature. The syndrome is characterized by the transformation of vaginal pain into a multi-organ system process. The pain is considerably greater and lasts longer than routine post-operative pain and treatment is extremely challenging.[10] The pain may continue, or even worsen, after mesh excision or revision. Completely new treatment modalities for pelvic pain have been developed as a response to this pain management challenge, including trigger point injections, nerve blocks, Botox injection, pelvic floor physical therapy, treatment with medications for chronic, neuropathic pain, and referral to contract-based pain management programs. These were extremely rarely used in urology or gynecology until the appearance of mesh-related pain.[11]

8. These and other complications may occur even in experienced hands and when proper surgical technique is used. Ethicon's marketing materials suggest that these complications occur mostly because of faulty surgical technique performed by inexperienced or poorly trained surgeons, perhaps by "over-tensioning" or misplacement. However, I have firsthand knowledge that is not the case. For example, I operated on one woman who had urethral erosion of synthetic mesh three years after it was implanted by one of our former fellows, whose expertise I am 100% confident of. Further, because of an unrelated episode of hematuria two years after implantation, she underwent cystoscopy which showed no signs of mesh erosion, yet one year later she was found to have erosion that also caused a urethral stricture. In the course of my practice, I have seen mesh complications from many world renowned experts, including physicians that Ethicon has retained as experts in litigation, and, from discussions with my colleagues, I know of many others. In the majority of cases that I see in my practice and that are reported in the literature, the device was placed in accordance with the manufacturers recommendations for placement.

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[9] E.g., ETH.MESH.00660488.

[10] E.g., Rogo-Gupta, 2013.

[11] E.g.,Petri, 2012; Rogo-Gupta, 2013; Ross S, Robert M, Swaby C, Dederer L, Lier D, Tang S, et al. Transobturator tape compared with tension-free vaginal tape for stress incontinence: a randomized controlled trial. Obstetrics and gynecology. 2009;114(6):1287-94; Cholhan HJ, Hutchings TB, Rooney KE. Dyspareunia associated with paraurethral banding in the transobturator sling. American journal of obstetrics and gynecology;202(5):481 e1-5; Boyles SH, Edwards R, Gregory W, Clark A. Complications associated with transobturator sling procedures. Int Urogynecol J Pelvic Floor Dysfunct. 2007;18(1):19-22; Parnell BA, Johnson EA, Zolnoun DA. Genitofemoral and perineal neuralgia after transobturator midurethral sling. Obstetrics and gynecology. 2012;119(2 Pt 2):428-31

9. Even the simplest complications are often more complicated than they appear. It is commonly stated that when there is extrusion of the mesh through the vaginal wall, it is quite a simple thing to just trim the edges of the exposed sling and either create small vaginal wall flaps to cover the defect or simply leave the wound open and apply estrogen. However, the studies that report successful outcomes generally have a short follow-up and the outcomes may be much worse than they appear.[12] In my own personal experience, I have seen many patients who were treated this way who came back months, years, and even decades later with more extrusions and granulomas that proved almost impossible to "cure."[13] These persistent and recurrent erosions are also reported in the medical literature and in Ethicon's own documents.[14]

10. Given the increasing number of mesh sling operations performed and the complexity of surgery to repair the complications, there are an increasing number of patients who have failed initial treatments and an increasing number of "mesh cripples". As more slings implantations are being performed and the longevity expectations of patients are increasing, it has become apparent that unanticipated, serious, and sometimes lifestyle- altering complications can occur that are not only unique to patients with slings but are also often refractory to treatment.[15] Other authors of recent peer-reviewed articles agree. Lee states that the use of synthetic material has generated novel complications, including mesh extrusion, pelvic and vaginal pain and mesh contraction, requiring a new classification system for complications relating to prosthesis insertion. He coined the term "Meshology" – an evolving field of sub-specialization dedicated to a growing population of affected women with complications from synthetic materials.[16] Barski also described mesh-related complications as "a current emerging problem, which confronts all urologists and gynecologists in their daily practice."[17]

11. Ethicon knew or should have known about these serious, potentially life-threatening complications and specifically designed another sling (TVT-O) to attempt to avoid them as well as compete in the marketplace.[18]

12. The retropubic approach, such as that described in the Gynecare TVT IFU and taught by Ethicon, increases the risk and incidence of bladder perforations, bowel perforations, and other disastrous intraoperative events.[19]

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[12] E.g., Blaivas, 2015

[13] E.g., Reynolds WS, Kit, L., Kaufman, M.R., Karram, M., Bales, G.T., and Dmochowski, R. Obturator Foramen Dissection for Excision of Symptomatic Transobturator Mesh. The Journal of Urology. 2012;187(5):1680-4.; Blaivas, 2013

[14] E.g., Petri, 2012; Abbott, 2014; Hansen, 2014; Unger, 2014; Rogo-Gupta, 2013; Shah , 2013; Dunn, 2014; Hammett, 2014; ETH.MESH.01706065 at 3.

[15] Blaivas 2015, 481.

[16] Lee 2015, 202.

[17] Barski and Deng 2015, p6.

[18] E.g., ETH.MESH.03932909.

[19] E.g., Brubaker, L., et al. (2011). "Adverse events over two years after retropubic or transobturator midurethral sling surgery: findings from the Trial of Midurethral Slings (TOMUS) study." Am J Obstet Gynecol 205(5): 498 e491-496; Deng, 2007; Olagundoye, V. O., et al. (2007). "Delayed presentation of small bowel trauma during insertion of tension free vaginal tape (TVT) sling." J Obstet Gynaecol 27(1): 92-93.

13. Claims that make the procedure sound as if it is safer and easier to perform than it actually is are misleading. See above. Ethicon's initial concept for this product was sound – a simple, safe, efficacious, outpatient procedure that required minimal surgical skills and could be mastered by surgeons with little training. But the reality of the Gynecare TVT is very different from this concept. It is not easy to learn these techniques and the ergonomics of the trocars is such that, even for the most skilled surgeon, it is easy to misguide them and end up in the wrong anatomical location. There is ample evidence in the literature that it is very common for the trocars to inadvertently puncture the bladder or urethra during trocar passage.[20]

14. There is little margin of error when placing a retropubic sling, such as the Gynecare TVT. The procedure involves the blind passage of trocars though the vagina and passing through or in close proximity to the following structures: bladder, bowels, anterior vaginal wall, arcus tendineus fascia pelvis, urethra, the obturator neurovascular bundle, and venous plexus of Santorini and then out two small incisions above the pubic bone. If it is located too superficially (i.e., between the vaginal epithelium and the pubocervical fascia), vaginal extrusion might occur. Conversely, a Gynecare TVT that is too deep (i.e., to the pubocervical fascia) can cause urethral or bladder erosion. In my experience training fellows and residents, I was struck by what a difficult time they had finding the correct plane, how much bleeding they got into during the dissection and how often they injured or almost injured the bladder or urethra during the dissection and/or passing the trocar. In fact, the bladder or urethra perforation occurred at a mean incidence of about 3% (range 0-16%).[21] Perforation of the bladder, bowel, urethra, or vagina during the original implantation surgery dramatically increases the risk of subsequent sling erosion 26 fold.[22]

15. Furthermore, the location of anatomical structures varies from individual to individual and even in the same individual, making accurate placement unpredictable. For example, positioning of the patient in various degrees of dorsal lithotomy position can impact the locations of nerves and blood vessels relative to surface landmarks. Further, the size of the obturator foramen and the bony pelvis can vary.[23] Since the Gynecare TVT normally passes dangerously close to vital structures, the anatomic and positional variations render trocar passage more hazardous than theoretic considerations would suggest.[24] Further, although bleeding can usually be controlled or is self-limited, nerve injuries can have disastrous long term consequences.

16. Removal of the Gynecare TVT-R is technically difficult and requires considerable surgical expertise that many implanting surgeons do not possess. Due to tissue ingrowth, it is very difficult

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[20] E.g., Bhoyrul S, Vierra MA, Nezhat CR, Krummel TM, Way LW. Trocar injuries in laparoscopic surgery. Journal of the American College of Surgeons. 2001;192(6):677-83; Shindel AW, Klutke CG. Urethral slings placed by the transobturator approach: evolution in the technique and review of the literature. Curr Urol Rep. 2005;6(5):385-92.

[21] E.g., Blaivas, 2015.

[22] E.g., *Id*., Osborn, D. J. et al. Analysis of patient and technical factors associated with midurethral sling mesh exposure and perforation. Int. J. Urol. 11, 1167–1170 (2014).

[23] E.g., Whiteside JL, Walters MD. Anatomy of the obturator region: relations to a trans-obturator sling. Int Urogynecol J Pelvic Floor Dysfunct. 2004;15(4):223-6; Litwiller JP, Wells RE, Jr., Halliwill JR, Carmichael SW, Warner MA. Effect of lithotomy positions on strain of the obturator and lateral femoral cutaneous nerves. Clinical anatomy. 2004;17(1):45-9.

[24] E.g., Bhoyrul, 2001; Shindel, 2005.

and sometimes impossible to remove the entire mesh and, in most instances, there are remnants of mesh that remain. This is well documented in the medical and scientific literature.[25] Further, there is a high likelihood of injuring adjacent structures and failing to alleviate symptoms, especially those related to pain, during removal surgery. There is a high incidence of recurrent sphincteric incontinence, requiring yet another procedure to repair it – ideally an autologous sling. Remnants of the partially removed Gynecare TVT-R can also migrate.[26] All of these procedures create more scar tissue in the pelvis, which further compromises the functionality of the pelvic anatomy and causes additional complications for women.

17. When the sling has been incorporated into the wall of the urethra or bladder, it is necessary to excise a portion of those structures in order to completely remove the mesh and, in so doing, there is a high likelihood of causing an urethrovaginal or vesicovaginal fistula. I have seen a number of such complications.[27] In order to prevent these fistulas, it is necessary to reconstruct the lower urinary tract and this usually requires considerable surgical expertise and experience utilizing plastic surgery techniques.[28]

18. When fistulas complicate mesh sling surgery, the outlook is grave. Although the reported incidence of mesh related fistulas is low (less than 1%), the success rate of surgical repair is low, 40% in our published experience. I have personally repaired approximately 200 vesicovaginal fistulas and approximately 150 urethrovaginal fistulas. With respect to fistula repair, I am only aware or seven failures in my series, four of whom were associated with mesh slings.[29]

19. The Gynecare TVT is not safer or less invasive overall than the alternative procedures. Furthermore, I have seen no evidence that Ethicon studied or evaluated the safety and efficacy of the insertion technique it developed and sold as part of the Gynecare TVT device or researched potential alternatives to minimize complications Even though the IFU says the procedure can be done under local anesthesia it also says it can be done using regional or general anesthesia. Ethicon knew that surgeons generally were more comfortable using general anesthesia and did not inform them that Ulmsten, the inventor of the device, had performed the procedure using local anesthesia and that using general anesthesia increased the risk of urinary retention and erosion and decreased the chance of successful outcomes for patients.[30]

20. Pubovaginal slings using autologous fascia are as effective as the Gynecare TVT. In my own personal series and according to several peer review meta-analyses and the AUA guideline panel the success rate for autologous slings is comparable to synthetic mesh slings.[31]

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[25] E.g., Blaivas, 2015; Blaivas, 2013; Shah, 2013.
[26] E.g., Blaivas, 2015
[27] E.g., Blaivas. 2014.
[28] E.g., Blaivas, 2008.
[29] E.g., Blaivas, 2014.
[30] E.g., ETH.MESH.04048515; ETH.MESH.00130934; ETH.MESH.00400955; Isenberg Dep., 11/6/13, 461:16-530:13; 553:15-554:21; 566:9-15.
[31] E.g., Ogah, J., Cody, D. J., & Rogerson, L. (2011). Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women: a short version Cochrane review. Neurourol Urodyn, 30(3), 284-291. doi: .1002/nau.20980; Wadie, B. S., Edwan, A., & Nabeeh, A. M. (2005). Autologous fascial sling polypropylene tape at

21. Pubovaginal slings using autologous fascia are safer than synthetic slings with respect to serious complications such as lifestyle altering pain, dyspareunia, vascular, erosion, bowel and lower urinary tract injury, and other complications. Although the reported incidence of urinary retention is slightly higher, much of the data to support that comes from an era before the importance of a tension free repair was known. Using current technique, urinary retention is comparable amongst autologous and synthetic slings.[32]

22. These types of serious complications do not occur or occur very rarely in the alternative surgical treatments for stress urinary incontinence (such as autologous fascia pubovaginal slings or the Burch procedure). Furthermore, when complications occur with pubovaginal slings using autologous fascia, they are easier to treat and rarely if ever result in the permanent, lifestyle altering complications mentioned above. In addition, when mesh is not involved, it is almost always possible to obtain a satisfactory result treating the complication, unlike the Gynecare TVT-R.[33]

23. In my own experience, performing thousands of rectus fascial slings, I have never injured the bladder, urethra, ureter or any adjacent organs except for two minor urethral injuries in women who had undergone multiple prior incontinence surgeries nor have we reported any nor have we reported any injuries in our case series.[34] Further, as a surgeon "of last resort" I have had the opportunity to care for at least a thousand women with complications of biologic slings, retropubic suspensions and vaginal repairs of incontinence and almost never have I seen complications of the magnitude of synthetic mesh sling complications that have become routine in my practice.

24. As a practicing surgeon, educator, academician, and editor/reviewer of scientific journals, I became aware of serious complications associated with synthetic mesh earlier than physicians in community practice. I first became aware of a death from a TVT sling approximately in 2000, but I already was including this fact in postgraduate lectures by 2002. The source of the information was first hand from the surgeon who performed the TVT. Industry (including Ethicon) representatives were present at meetings in which these complications were discussed by me and my colleagues. In addition, case reports appeared in the literature relatively soon after introduction of these devices and before clinical trials were completed. Further, complications appeared in the MAUDE database. As evidenced by Ethicon's written materials, Ethicon downplayed these complications.

25. There is almost always a time lag between what is known by Industry and physicians such as myself and community physicians. This is due to the time it takes for the dissemination of information and the withholding of information by Ethicon. Community doctors are often unable to keep up with the vast amount of and rapid changes in the scientific literature. They generally rely on manufacturers, through their sales and other representatives, to provide complete and

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short-term followup: a prospective randomized study. J Urol, 174(3), 990-993. doi: .1097/01.ju.0000169492.96167.fe; Garcia-Urena, 2007

[32] E.g., Blaivas, J. G., & Chaikin, D. C. (2011). Pubovaginal fascial sling for the treatment of all types of stress urinary incontinence: surgical technique and longterm outcome. Urol Clin North Am, 38(1), 7-15, v. doi: .1016/j.ucl.2010.12.002; Garcia-Urena, 2007.

[33] E.g., Blaivas, 2011; Blandon, R., Gebhart, J., Trabuco, E., & Klingele, C. (2009). Complications from vaginally placed mesh in pelvic reconstructive surgery. Int Urogynecol J 20, 523-531. doi: 10.1007/s00192-009-0818-9.

[34] E.g., Blaivas, 2011.

accurate information to them. Based on my interactions with company representatives (including Ethicon), and company (including Ethicon) promotional materials, synthetic slings were invariably described as effective, quick, having few complications, and easy to learn and perform.

26. Mesh complications are significantly under-reported.[35] Additionally many, if not most, patients who experience complications do not return to their original implanting surgeons, contributing to a misperception among individual physicians that their outcomes are better than they, in fact, are.

27. The overall risk of a negative outcome after SMUS implantation surgery is ≥ 15%.[36] We calculated these minimum risks: revision surgery for erosion and obstruction alone, 4.1%; chronic pain, 4.1%; recurrent or persistent SUI, 5.3%; and *de novo* refractory OAB 3.9%. Of note, in patients requiring mesh removal, recurrence of SUI has been reported in 10–60% of individuals. Transobturator sling complications differed from retropubic sling complications in type and severity.

28. Despite the limitations in determining the exact rate of MSUS complications, other researchers have come up with similar rates in recent literature. Barski and Deng reported that "the rate of mesh-related complications is about 15–25% and mesh erosion is up to 10% for POP and SUI repair. Mesh explantation is necessary in about 1-2% of patients due to complications."[37] Lee reported the incidence of chronic/persistent pain following MUS placement varies from 0 to 30%. The authors cited that Petri and Ashok reported on the management of 280 cases of late sling complications (RP 210 and TO 70). Compared with the retropubic MUS group, the TOT group had greater number of complications related to persistent pain (10% TVTs vs 32% TOT tapes), dyspareunia (3 vs 18%) and tape-related infections (4 vs 18%).[38] These rates are in keeping with those reported in Nature.

29. Ethicon did not adequately warn doctors and patients about the possibility of serious, chronic and lifestyle altering nature of the complications associated with its products, such as the Gynecare TVT, which included chronic and debilitating pain, chronic dyspareunia and sexual dysfunction, nerve injuries/entrapment, groin and leg pain, vaginal scarring, bladder dysfunction, bladder stones, recurrent urinary or bladder infections, recurrence, refractory overactive bladder and refractory sphincteric incontinence, the need for multiple corrective surgeries that may not resolve the symptoms, the marked difficulty removing the mesh sling and that even worse complications may ensue from mesh removal, the difficulties that occurred in treating the

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[35] E.g., Deng, 2007; Anger JT, Litwin, M. S., Wang, Q., Pashos, C. L., & Rodriguez, L. V. . Complications of sling surgery among female Medicare beneficiaries. Obstetrics & Gynecology. 2007;109(3):707-14; Blaivas, 2015; Dunn, 2014

[36] Evaluating the incidence, severity and consequences of the various RP and/or TOT sling complications is a daunting task. The reasons are varied include factors such as the failure of most of the thousands of articles regarding SMUS to track complications in any meaningful way; short-term follow-up and patients lost to follow-up; new, previously unrecognized complications such as banding as a cause of dyspareunia; absence of severity descriptions of pain; different complication profiles with different slings; and failure to address outcomes (including recurrent SUI) following corrective surgeries.

[37] Barski and Deng 2015, 2.

[38] Lee 2015, 205.

worsening of SUI following sling removal, and others.[39] Ethicon did not adequately warn physicians about the possibility that the complications above, including erosion, could occur months or years after placement of a synthetic sling, such as the Gynecare TVT.[40]

30. Ethicon did not adequately warn doctors and patients about the difficulty removing their products, such as the Gynecare TVT, nor did it warn them about the suboptimal and unpredictable results when mesh excision or revision becomes warranted due to complications. Very significantly, Ethicon did not attempt to train or educate doctors on how to best treat complications when they occur.[41]

31. The design of the Gynecare TVT is flawed because the product IFU does not accurately represent the nature of the inflammatory response and resulting scar tissue. Instead, the pre-2015 TVT IFUs state that "animal studies show that implantation of PROLENE mesh elicits a minimal inflammatory reaction in tissues, which is transient and is followed by the deposition of a thin layer of tissue, which can grow through the interstices of the mesh, thus incorporating the mesh into adjacent tissue. The material is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes." Although Ethicon changed this language in January 2015 to remove the term “transient”, it did not alert physicians that: (1) the mesh creates dense scar tissue not a "thin layer of tissue;" or (2) that the mesh is subject to degradation and weakening upon implantation.[42]

32. The design of the TVT-R is also flawed because the product’s IFU does not accurately and completely represent the nature of the potential complications that women can suffer. It simply lists an almost encyclopedic number of adverse events with a kind of equanimity that minimizes the impact on patients and conveys to the doctor the impression that although these things might occur, they are very rare. For example, it states that one or more revision surgeries may be necessary but does not mentioned the well-known fact that these operations can be very difficult to do, requires great expertise and the results are often sub optimal. Further, the IFU does not even mention the severity and life style altering nature of some of these complications.

33. In addition, the IFU incorrectly states that the TVT-R is “tension-free.” In reality, it is extremely difficult to correctly “tension” the sling. If placed even slightly too snugly, the tape may cause temporary or permanent lower urinary tract obstruction. This is compounded and the problems increase over time as the TVT-R shrinks in a woman’s body. On the other hand, if the sling is applied too loosely, incontinence will persist.

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[39] E.g., ETH.MESH.03427878; ETH.MESH.02340504; ETH.MESH.05222673; ETH.MESH.02340471; ETH.MESH.02340306; ETH.MESH.05225354.

[40] E.g., *Id.*

[41] Blaivas, 2013; Unger, C., Abbot, S., Evans, J., Jallad, K., Mishra, K., Karram, M., Iglesia, C., Rardin, C., Barber, M. Outcomes following treatment for pelvic floor mesh complications. *Int Urogynecol J.* DOI 10.1007/s00192-013-2282-9.

[42] E.g., ETH.MESH.05588123; Barbolt Dep. 01/08/14, 409; 516-17; Hinoul Dep. 4/5/12 99:09-25; 4/6/12 518:14520:20; 6/26/13 175:1-176:17,;184:18-22; 328:10-24; Owens Dep. 9/12/2012 98:11-99:07; ETH.MESH.00870466; ETH.MESH.01218361; Holste Dep. 7/29/13 51:3-53:6; Vailhe Dep. 6/21/13 383:8-19; 1/2015 TVT IFU from Ethicon website.

34. The pre-2015 IFUs are also inadequate in that it represents complications as "transitory":

> Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation or inflammation.[43]

This language is not correct – the complications can be permanent, not transitory as Ethicon states. I agree with Ethicon's Associate Medical Director of Worldwide Customer Quality Meng Chen, M.D., who stated "Pardon me again, from what I see each day, these patient experiences are not "transitory" at all."[44] Although this language was deleted in January 2015 and replaced with language that reads "Neuromuscular problems, including acute and/or chronic pain in the groin, thigh, leg, pelvic and/or abdominal area may occur," this language was added too many years after Ethicon was aware of the chronic nature of the problems women can experience and still does not adequately warn physicians and patients about the complications associated with the TVT-R device.

35. Published reports on long-term outcomes of patients after mesh removal surgery are limited. Most authors of studies in this area commented on the technical difficulties encountered during mesh excision surgery and the fact that many (and in some series, most) patients require two or more surgeries; thus, even in the short term, outcomes are often suboptimal. Beyond the immediate intra-operative risks lays ahead the concern for secondary urinary incontinence and its management. At least one-third of patients undergoing sling excision surgery develop recurrent SUI. Treatment of persistent pain in patients with a SMUS is particularly challenging and has been entirely empirical and progressive in nature. Chronic disabling pain is one of the most common indications for mesh removal[45] Barski also described the difficulty treating pain caused by mesh slings with only 28% reporting a relief of symptoms postoperatively. Particularly difficult and traumatic for the pelvic floor were the excisions of transobturator tapes, according to the Barski review.[46] Lee also described pelvic pain and dyspareunia (up to 24% following MUS) as a "most distressing and potentially irreversible complication to treat."[47] The etiology of chronic pain after MUS surgery is multifactorial. A complex interplay of factors can be causative, including synthetic material type, nerve and muscle injury, infection, con- traction, erosion or extrusion.[48]

36. Ethicon would have known about these serious complications if proper clinical trials had been performed. Appropriate and unbiased clinical testing, if performed, would have shown the problems and complications associated with synthetic slings, like the Gynecare TVT-R. Because of the known complications, many occurring years after the original surgery, well conducted, long term clinical trials (or a registry) would have demonstrated the extent and nature of these devastating complications.

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[43] ETH.MESH.03427878; ETH.MESH.02340504; ETH.MESH.05222673; ETH.MESH.02340471; ETH.MESH.02340306; ETH.MESH.05225354. *Also* Weisberg dep. (8/9/13) 968:2-969:10; Robinson Dep. (9/11/13) 329:12-330:7

[44] ETH.MESH.04093125.

[45] Blaivas 2015, 494.

[46] Barski and Deng 2015, p6.

[47] Lee 2015, 2

[48] Lee 2015, 205.

37. The medical literature surrounding the Gynecare TVT-R and other synthetic slings, is seriously flawed for reasons including, but not limited to, industry sponsorship, researcher bias, publication bias, industry manipulation of data, inappropriate choice of outcome variables, and lack of long-term follow-up.[49] In the Nature review, we noted the poor quality of many of the studies assessing risks of SMUS-associated complications. Deficiencies include the absence of sufficiently explicit outcome data due to the validation instruments used, the lack of long-term data, the loss of patients to follow-up, and the failure to distinguish between different products - to name a few. The poor quality of many of the studies on SMUS has been confirmed by other authors as well. Brubaker reported on missing data in two large SUI trials, TOMUS and SISTer.[50] Barski, in performing the meta-analysis on mesh complications, found no randomized trials on the surgical treatment of mesh complications and also decried the poor quality of the studies.[51]

38. Ethicon would have known about these serious complications if proper clinical trials had been performed. Appropriate and unbiased clinical testing, if performed, would have shown the problems and complications associated with synthetic slings, like the Gynecare TVT. Because of the known complications, many occurring years after the original surgery, well conducted, longterm clinical trials (or a registry) would have demonstrated the extent and nature of these devastating complications.

39. The medical literature surrounding the Gynecare TVT and other synthetic slings, is seriously flawed for reasons including, but not limited to, industry sponsorship, researcher bias, publication bias, industry manipulation of data, inappropriate choice of outcome variables, and lack of long-term follow-up.[52] For example, internal Ethicon documents included a contract between Ethicon and Medscand Medical A.B. in which it was to receive payment contingent upon certain predetermined study outcomes. Payments to Medscand were conditioned upon the completion of studies by a predetermined date.[53] According to the agreement, Ethicon was the owner of any of work resulting from Ulmsten's studies.[54] The contract and payments were subject to Ulmsten's results regarding perioperative and postoperative complications, efficacy, and safety not varying "significantly" from Ulmsten's original publication (Int. Urogynecol J 1996-7:81-86).[55] The data used by Ulmsten and Nilsson in their initial and follow up publications was flawed and they failed to disclose the unexplained patient loss to follow up and an adverse event.[56] The 5-year follow up study also fails to report the patient loss to follow up or explain why only three of the original six centers were being included.[57] The 17-year follow up authored by Nilson also had a significant loss to follow up and only 51% of patients were evaluated in person.[58]

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[49] E.g., Blaivas, 2015; ETH.MESH.00262089; ETH.MESH.00658508; ETH.MESH.03918253

[50] Brubaker L, et al. Missing data frequency and correlates in two randomized surgical trials for urinary incontinence in women. Int Urogynecol J. 2015; 26:1155-1159.

[51] Barski D and Deng DY. Management of mesh complications after SUI and POP repair: Review and analysis of the current literature. Biomed Res Int. 2015;2015:831285, p2. Doi: 10.1155/2015/831285. [Epub 2015 Apr 20].

[52] E.g., Blaivas, 2015; ETH.MESH.00262089; ETH.MESH.00658508; ETH.MESH.03918253.

[53] E.g., ETH.MESH.08696084.

[54] E.g., ETH.MESH.08696084 at 08696116.

[55] E.g., ETH.MESH.08696084 at 08696132.

[56] E.g., ETH.MESH.00371496 at 00371587; Ulmsten data; Nilsson Int Urogynecol J 2001.

[57] E.g., *Id.*

[58] E.g., Blaivas, 2015.

Furthermore, a randomized study involving the TVT reported significantly lower objective success rates than those reported by Ulmsten and Nilsson.[5960]

40. Many authors have signed contracts with mesh manufacturers and have acted as paid consultants for mesh manufacturers. These contracts often contain language that prevents company consultants from reporting or discussing device complications without written company approval. In some articles, these conflicts are not disclosed.[61]

41. Endorsement of these products by professional societies (e.g. the AUGS and SUFU Guidelines Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence) is biased because presents a one sided perspective. These paper cite the safety and efficacy of mesh slings, yet never even mentions the word complication. Further there is no conflict of interest statement or disclaimer despite the fact that several of the authors of the papers have financial interests with from mesh manufacturers.[62]

42. Underreporting of SMUS complications is also well-documented in the medical literature and discussed in the Nature article. Discrepancies exist between the SMUS complication rates reported by urologists from individual institutions, those reported in the literature, the (unreported) experience of tertiary care practices and those in the MAUDE (Manufacturer and User Facility Device Experience) database.[63] In our Nature review, we determined that approximately 88,000 removal surgeries should have been performed (based on published rates), and yet only a small fraction of such procedures are reported in the peer-reviewed literature.[64] Use of imperfect research methodologies, a lack of long-term follow up and reporting bias have been suggested as causes of these differences.[65]

43. Some authors and key opinion leaders have signed contracts with mesh manufacturers and have acted as paid consultants for mesh manufacturers. These contracts often contain language that prevents company consultants from reporting or discussing device complications without written company approval. In some articles, these conflicts are not disclosed.[66]

44. The Prolene mesh in the TVT-R can be either Mechanically Cut (MCM) or Laser Cut (LCM) in the manufacturing process.[67] Each carries its own unique problems for women.

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[59] E.g., Albo, M. et al. Treatment success of retropubic and transobturator mid urethral slings at 24 months. J. Urol.
[60] , 2281–2287 (2012).
[61] E.g., ETH.MESH.00262089; ETH.MESH.08692936; ETH.MESH.02123291; ETH.MESH. 8696084.
[62] E.g., ETH.MESH.04982735; ETH.MESH.05125268; ETH.MESH.05342590; ETH.MESH.09143435; ETH.MESH.04982748; ETH.MESH.08073794; ETH.MESH.08073801; ETH.MESH.08307690; ETH.MESH.09293114.
[63] Blaivas 2015, 481-509, 484.
[64] Blaivas 2015, 481-509, 485.
[65] Blaivas 2015, 481-509, 485.
[66] E.g., ETH.MESH.00262089; ETH.MESH.08692936; ETH.MESH.02123291; ETH.MESH.08696084
[67] ETH.MESH.09951087; Deposition of Dan Smith, May 15, 2014, 48:11-17

45. MCM can cause problems of fraying and deformation. Numerous complaints of the Gynecare TVT fraying and deforming during the implantation were reported to Ethicon.[68] Between launching the Gynecare TVT and November of 2003, Ethicon received 58 such complaints. According to these complaints, the fraying became more apparent when the color of the Gynecare TVT was changed from clear to blue.[69] Physicians also reported to Ethicon that the "crumbling" of the Gynecare TVT was worsened when the product was stretched or when the protective sheaths were removed during surgery.[70] An Ethicon engineer stated the "root cause" of the particle loss was the mechanical cutting of the polypropylene mesh and that changing the method of cutting could significantly limit the fraying of the mesh.[71] Ethicon documents confirm that the particle loss for the mechanical cut Gynecare TVT-R rates higher than the synthetic slings of other manufacturers.[72]

46. The polypropylene mesh used in the Gynecare TVT deforms *in vivo*. The deformation includes curling, cording, roping, rolling, deformation, loss of pore size with tension, and fraying. This deformation leads to pain and contracture and other complications.[73] Ethicon documents clearly illustrate the Gynecare TVT roping, curling and deforming when subjected to tension or elongation.[74] The roping, curling, deformation, particle loss and degradation was greater with the mechanically cut mesh than with the laser cut mesh.[75]

47. The mechanically cut Gynecare TVT also has "sharp edges", which can cause adverse clinical complications in women such as erosion and abrasions and others.[76] Ethicon also received concerns from physicians that these sharp edges were causing complications in patients, including increased erosions.[77]

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[68] E.g., ETH.MESH.03905472; ETH.MESH.02621559; ETH.MESH.01813975; ETH.MESH.05644163; ETH.MESH.01809082.

[69] E.g., ETH.MESH.00541379; ETH.MESH.00863391; ETH.MESH.02180833; ETH.MESH.02180828.

[70] ETH.MESH.00858252

[71] E.g., ETH.MESH.01813975.

[72] ETH.MESH.01221055; ETH.MESH.00585842; ETH.MESH.01219629; ETH.MESH.01221024; ETH.MESH.00585823

[73] E.g., Klinge, 1998 (Shrinking); Feiner, 2010; Ostergard DR. Lessons from the past: directions for the future. Do new marketed surgical procedures and grafts produce ethical, personal liability, and legal concerns for physicians? Int Urogynecol J Pelvic Floor Dysfunct. 2007;18(6):591-8; Jacquetin, 2009; Tunn R, Picot A, Marschke J, Gauruder-Burmester A. Sonomorphological evaluation of polypropylene mesh implants after vaginal mesh repair in women with cystocele or rectocele. Ultrasound in obstetrics & gynecology: the official journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2007;29(4):449-52.

[74] E.g., ETH.MESH.00294195 (Moalli, P. A., et al. (2008). "Tensile properties of five commonly used mid-urethral slings relative to the TVT." Int Urogynecol J Pelvic Floor Dysfunct 19(5): 655-663); ETH.MESH.00440005; ETH.MESH.00302390.

[75] E.g., ETH.MESH.08334245; ETH.MESH 00440005; ETH.MESH 00302390.

[76] E.g., ETH.MESH.09656790.

[77] E.g., ETH.MESH.06696589; ETH.MESH.00330760; ETH.MESH.03911107; ETH.MESH.02620354; ETH.MESH.02625055; ETH.MESH.02653814; ETH.MESH.02652985; ETH.MESH.03715978; ETH.MESH.02630134; ETH.MESH.02628698; ETH.MESH.02626378; ETH.MESH.02622954; ETH.MESH.02622456; ETH.MESH.18882038

48. LCM means that the plastic mesh is cut into strips using a laser instead a cutting blade.[78] The result is that the mesh itself is stiffer than mechanically cut mesh. In fact, an internal memo from Becky Leibowitz to Paul Parisi and Dan Smith in late 2004 found that when the laser cut mesh was stretched it became about three times stiffer than the machine-cut TVT mesh.[79] Just four years later, in meeting notes, it is noted that there is a consensus that laser cut mesh is more rigid and stiff and that no clinical study has been done regarding the differences between laser cut mesh and mechanical cut mesh. The notes further indicate potential benefits of using mechanical cut mesh over laser cut mesh noting a lower rate of erosions, tensioning would be more similar to current products, and the edges of mechanical cut mesh might allow for an easier insertion.[80]

49. Importantly, most surgeons using the TVT products did not know what type of mesh (LCM or MCM) they were using.[81] Thus, there is no way for doctors to adjust tensioning differently or be aware that the mesh is stiffer, or to warn patients of an increased risk of erosions. The difference in the stretch profile between mechanically cut and laser cut mesh also led Carl G. Nilsson and Christian Falconer, two of the inventors of the original TVT,[82] and Jean de Leval, the inventor of TVT-O, to refuse to use, and question the use, of laser cut mesh.[83]

50. Moreover, use of the laser cut mesh would make them unable to rely on the original studies and data they use to tout the safety and effectiveness of the original TVT.[84] This data is something Ethicon wanted to rely on for all TVT-R products.[85] Additionally, laser cut mesh was never assessed on its own in a clinical trial.[86] Finally, the rigidity of the laser cut mesh can cause a higher incidence of erosion and sexual dysfunction than mechanically cut mesh.[87]

51. It is well established in the medical and scientific literature that heavier weight, smaller pore sized mesh such as that used in the Gynecare TVT-R elicits a greater inflammatory and fibrotic reaction in women.[88]

52. Despite moving to a lighter weight, larger pore sized mesh for its hernia products in the late 1990's and for its pelvic organ prolapse products so as to minimize the body's inflammatory and foreign body reaction to the polypropylene devices, Ethicon continued to manufacture the Gynecare TVT-R from the heavier weight, smaller pore sized mesh, ignoring the increased risks to patient safety and product efficacy.[89]

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[78] Lamont Dep. (9/11/13) 12:13-13:14
[79] ETH.MESH.01809080
[80] ETH.MESH.03916716
[81] ETH.MESH.09911296; ETH.MESH.09951087
[82] ETH.MESH.16416002, ETH.MESH.04048515
[83] ETH.MESH.03916716
[84] ETH.MESH.06040171; ETH.MESH.01706065
[85] Trial Testimony of Katrin Elbert, *Perry v. Luu, et al.*, (2/11/15) 3328-30
[86] ETH.MESH.03941617
[87] ETH.MESH.00294195; ETH.MESH.03916716; ETH.MESH.01706065; ETH.MESH.03923121
[88] E.g., Klinge U, Junge K, Stumpf M, Ap AP, Klosterhalfen B. Functional and morphological evaluation of a lowweight, monofilament polypropylene mesh for hernia repair. Journal of biomedical materials research; 63(2):129-36; Klosterhalfen, 2005.
[89] E.g., ETH.MESH.07455220; ETH.MESH.09275875; ETH.MESH.02268619; ETH.MESH.02589032; ETH.MESH.01264260; Smith Dep. (2/3/2014) 723:9-724:6, 829:16-829:19; Burkley Dep. (5/22/13) 184:17-24

53. The Gynecare TVT-R should not have been designed for permanent implantation in the human body without proper animal and human studies because the polypropylene used therein can elicit a permanent and persistent inflammatory response[90] and can create dense scar tissue.[91] Ethicon internal documents confirm it was aware of problems contemporaneously.[92]

54. The polypropylene mesh used in the Gynecare TVT-R creates scar plate that can entrap nerves, smooth muscle, and striated muscle and causes other tissue abnormalities.[93] Pore size, density, weight and surface area are all factors involved in scar plate formation.[94] This increased scar plate formation has adverse clinical consequences in women, including distortion of the pelvic anatomy, chronic pain, dyspareunia and/or sexual impairment, bladder and/or bowel dysfunction and other complications. These forces can act on the entire structure of the Gynecare TVT-R.[95]

55. The polypropylene mesh used in the Gynecare TVT-R shrinks unpredictably and asymmetrically, influenced by individual response, bacterial contamination, anatomical location, and time.[96] Because of and the unpredictable amount of shrinkage, it is not possible for the surgeon to determine the proper amount of tension to apply and there is no procedure that is really reliably "tension-free". The consequences of mesh shrinkage are very significant, resulting in pain, dyspareunia, urinary symptoms, and other complications.

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[90] E.g., Klinge , 1998 (Shrinking):965-9; Clave, A., Polypropylene as a Reinforcement in Pelvic Surgery is Not Inert: Comparative Analysis of 100 Explants, I Urogynecol J, 2010 21:261-270; Klinge U, Klosterhalfen B, Muller M, Schumpelick V, "Foreign Body reaction to Meshes Used for the Repair of Abdominal Wall Hernias,"; Eur J Surg, 1998 (164:951–960); Klostherhalfen,B, Junge, K, Klinge, U, "The lightweight and large porous mesh concept for hernia repair," Expert Rev. Med. Devices, 2005 2(1); Binnebosel M, von Trotha K, Jansen P, Conze J, Neumann U, Junge K, "Biocompatibility of prosthetic meshes in abdominal surgery" Semin Immunopathol, 2011 (33:235-243).

[91] E.g., Heise, C. P., & Starling, J. R. (1998). Mesh inguinodynia: a new clinical syndrome after inguinal herniorrhaphy? Journal Of The American College Of Surgeons, 187(5), 514-518; Demirer, S., Kepenekci, I., Evirgen, O., Birsen, O., Tuzuner, A., Karahuseyinoglu, S., & Kuterdem, E. (2006). The effect of polypropylene mesh on ilioinguinal nerve in open mesh repair of groin hernia. The Journal Of Surgical Research, 131(2), 175-181; Klosterhalfen, 2005; Klinge, 1998 (Shrinking).

[92] E.g., Burkley Dep. (5/22/13) 184:17-24; ETH.MESH.05588123; Hinoul Dep. (4/5/12) 99:09-25; (4/6/12) 518:14-520:20; (6/26/13) 175:1-176:17;184:18-22; 328:10-24; Owens Dep. (9/12/2012) 98:11-99:07.

[93] E.g., Heise, 1998; Demirer, 2006; Klosterhalfen, 2005; Vervest, H., Bongers, M. & van der Wurff, A. Nerve injury: an exceptional cause of pain after TVT. Int. Urogynecol. J. Pelvic Floor Dysfunct. 6, 665–667 (2006); Iakovlev V., M. G., Blaivas J. (2014). "Pathological Findings of Transvaginal Polypropylene Slings Explanted for Late Complications: Mesh is Not Inert [Abstract]." International Continence Society Meeting Annual Meeting; ETH.MESH.01264260.

[94] E.g., Iakovlev, 2014; ETH.MESH.01264260

[95] E.g., Blaivas, J. G., et al. (2015). "Safety considerations for synthetic sling surgery." Nat Rev Urol

[96] E.g., Klinge, 1998 (Shrinking); Feiner B, Maher C. Vaginal mesh contraction: definition, clinical presentation, and management. Obstetrics and gynecology. 2010;115(2 Pt 1):325-30; Mamy L, Letouzey V, Lavigne JP, Garric X, Gondry J, Mares P, et al. Correlation between shrinkage and infection of implanted synthetic meshes using an animal model of mesh infection. Int Urogynecol J. 2011;22(1):47-52; Letouzey V, Huberlant S, Lavigne J, Mares P, Garric X, De Tayrac R. Is polypropylene mesh coated with antibiotics is efficient to prevent mesh infection and contraction in an animal infectious model? [Abstract]. 37th Annual Meeting of the International Urogynecological Association. 2012:193; Jacquetin B, Cosson M. Complications of vaginal mesh: our experience. Int Urogynecol J Pelvic Floor Dysfunct. 2009;20(8):893-6; Garcia-Urena MA, Vega Ruiz V, Godoy A, Baez Perea JM, Marin Gomez LM, Carnero Hernandez FM, et al. Differences in polypropylene shrinkage depending on mesh position in an experimental study. Am J Surg. 2007;193(4):538-42

56. In the Nature paper, we discussed the mechanisms for mesh-related complications. These include inflammatory reactions, fibrosis, deformation, nerve entrapment, degradation, shrinkage/contraction, migration, and stiffening. These material features of polypropylene mesh and their relationship to mesh complications are discussed in my expert report. Numerous recent peer-reviewed articles have confirmed the contribution of these properties into the mechanisms of mesh-related symptoms for patients.

57. Degradation was reported in papers by Iakovlev et. al and Imel et. al on the in vivo degradation of transvaginally implanted polypropylene products. Degradation progresses over time and results in clinically significant embrittlement, loss of flexibility mesh stiffening and deformation.[97,98] Bendavid reported on the mechanism of hernia mesh repair pain. This new clinical syndrome, characterized by slow onset, relentless progression, and uncompromising lack of response to treatment, was attributed to nerve entrapment incased in dense scar tissue. According to the author, the pores of mesh need to be viewed as "mini-compartments" of biological tissue where the vasculature, nerves and their receptors are exposed to potential mechanical and chemical factors: scarring, entrapment, compression, tugging, deformation, contraction, hypoxia/acidosis, inflammation and edema.[99] In another study by Bendavid et. al, a marked increase in nerve density trapped in scar was observed in patients who had mesh-related pain, regardless of the surgical technique or surgical location.[100] Testing by Lee also discussed the mechanisms of chronic pain after MUS surgery, describing a "complex interplay of factors [that] can be causative, including synthetic material type, nerve and muscle injury, infection, contraction, erosion or extrusion."[101]

58. Questions have been raised in the peer-reviewed literature regarding the carcinogenic potential for transvaginally placed polypropylene mesh. We addressed this concern in our Nature review. These carcinogenic effects, leading to the development of sarcomas, have been studied in animal models. The basic research and clinical data suggest that implantation of polypropylene mesh might increase the risk of sarcoma. If a risk is present in humans, it is likely to be very low. Mutagenic effects, in general can take many years to accumulate and then a long period to cause a neoplasm. Detecting any oncogenic effects of SMUS implants would require a large cohort of patients with the same type of implant, and these patients would have to be followed up for a sufficiently long period of time, most likely at least 15 years. [102] However, a recent case of clear cell carcinoma associated with an eroded polypropylene sling was reported November, 2015 in the International Urogynecology Journal.[103] A second case of squamous cell carcinoma associated with a midurethral sling was reported at the same time. In an accompanying editorial in the same

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[97] Iakovlev VV, et al. Degradation of polypropylene in vivo: A microscopic analysis of meshes explanted form patients. 2015:00B:000-000, p10.
[98] Imel A, et al. In vivo oxidative degradation of polypropylene pelvic mesh. Biomaterials. 2015 Dec;73:131-41, 132.
[99] Bendavid R, et al. Mesh-related SIN syndrome. A surreptitious irreversible neuralgia and its morphologic background in the etiology of post-herniorrhaphy pain. Int J Clin Med. 2014; 5:799-810, 799.
[100] Bendavid R, et al. A mechanism of mesh-related post-herniorrhaphy neuralgia. Hernia. 2015 Nov 23, p6. [Epub ahead of print].
[101] Lee 2015, 205.
[102] Blaivas 2015, 481-509, 500.
[103] Lin HZ, et al. A first reported case of clear cell carcinoma associated with delayed extrusion of midurethral tape. Int Urogynecol J. 2015 Nov 20. [Epub ahead of print].

journal issue, Goldman recognized that a cause-and-effect pattern could be concerning and recommended vigilance.[104] This is new information that supports my opinions that patients who receive mesh products should be monitored closely over a long-term period.

59. I have reviewed the Material Safety Data Sheet for the polypropylene used in the Gynecare TVT-R medical device and related documents. This document states in part, under INCOMPATIBILITY, that the following materials are incompatible with this product: Strong oxidizers such as chlorine, peroxides, chromates, nitric acid, perchlorates, concentrated oxygen, sodium hypochlorite, calcium hypochlorite and permanganates. Chlorine; Nitric acid.[105] The Gynecare TVT-R should not have been designed using this polypropylene because many of these chemicals are routinely found in human tissue.

60. The polypropylene mesh used in the Gynecare TVT-R degrades *in vivo*.[106] Degradation has been reported to result in stiffening of the mesh and the presence of small molecular complexes and chemical products of degradation in surrounding tissues provides an additional stimulus for the chronic inflammatory response, which causes a continuous cycle of remodeling around the mesh filaments and extension of fibrosis.[107] *In vivo* it has been well documented that mesh also stiffens.[108] Dr. Iakovlev and I have recently published an abstract in a peer-review journal that describes mesh hardening, degradation, deformation, and nerve/muscle entrapment from a histological standpoint and how these findings relate to pain and other mesh complications.[109]

61. Ethicon's own internal document support my opinion that polypropylene mesh degrades in the body.[110]

All opinions are given to a reasonable degree of medical certainty. I reserve the right to amend or supplement this report if additional information becomes available. I also reserve the right to adopt all of my opinions in the other reports that I have submitted for the Wave 1 cases.

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[104] Goldman HB and Dwyer. Polypropylene mesh slings and cancer: An incidental finding or association? Int Urogynecol J. 2015 Nov 19, p2. [Epub ahead of print].

[105] ETH.MESH.02026591.

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[108] E.g., Costello, 2007 (Materials); Fayolle B, Audouin L, Verdu J. Oxidation induced embrittlement in polypropylene - a tensile testing study. Polymer Degradation and Stability. 2000;70(2000):333-40; Fayolle B, Audouin L, Verdu J. Initial steps and embrittlement in the thermal oxidation of stabilised polypropylene films. Polymer Degradation and Stability. 2002;75:123-9; Fayolle B, Audouin L, George GA, Verdu J. Macroscopic

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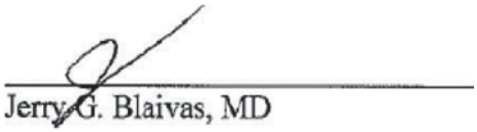
[110] ETH.MESH.07690752; DEPO.ETH.MESH.00004755; ETH.MESH.12831391; ETH.MESH.02589032; ETH.MESH.07192929; ETH.MESH.01264260; Burkley Dep., May 23, 2013 at 315:8-13.

This 1st day of February, 2016.



Jerry G. Blaivas, MD

III. FACTS OR DATA CONSIDERED IN FORMING OPINIONS

In addition to the references included herein, an Index is attached hereto and by reference made a part hereof. Please see **Exhibit "C"** attached.

IV. COMPENSATION

Dr. Blaivas' Fee Schedule is attached hereto and by reference made a part hereof. Please see **Exhibit "B"** attached.

V. LISTING OF CASES IN WHICH TESTIMONY HAS BEEN GIVEN IN THE LAST FOUR YEARS

Merjem Delija v. Neil Sayegh, etc.; index no. 14449/2003

Jose Cuevas v. the Mount Sinai medical Center; Index no. 0017209/2004

Randy Smith, et al. v. Andrew Chan, M.D., et al.; Index No. 024786/2009

Katelyn Vercher, et al. v. Chiari Institute, et al.; 2:09-cv-01751-AKT

Lisa Marie Fontes, et al. v. American Medical Systems, Inc.; 2:12-CV-02472

Debbie Jilovec, et al., v. American Medical Systems, Inc.; 2:12-CV-05561

Joann Serrano, v. American Medical Systems, Inc.; 2:12-CV-3719

Mary Weiler, et al. v. American Medical Systems, Inc.; 2:12-CV-05836

Carolyn F. Smothers v. Boston Scientific Corp.; 2:12-cv-08016

Katherine L. Hall v. Boston Scientific Corp.; 2:12-cv-08186

Julia Wilson v. Boston Scientific Corp.; 2012-02626

Ronda Orozco, et al., v. Boston Scientific Corp.; 2012-03068

Maria Cardenas v. Boston Scientific Corp.; 2012-02912

Diane Albright v. Boston Scientific Corp.; 2012-00909

Jo Huskey, et. al v. Ethicon, Inc.; 2:12-cv-05201

Tonya Edwards, et. al v. Ethicon, Inc.; 2:12-cv-09972